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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/898,751	07/02/2001	Wei Wang	DX0882XK	7429

7590 11/29/2002

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EXAMINER	
BUNNER, BRIDGET E	

ART UNIT	PAPER NUMBER
1647	12

DATE MAILED: 11/29/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/898,751	WANG ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,22 and 23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,22 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *9* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 23 September 2002 (Paper No. 11) has been entered in full. Claims 5-21 are cancelled and claims 1-4 and 22-23 are amended.

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-4 and 22-23, drawn to a method of modulating movement of a cell within the skin of a mammal in Paper No. 11 (23 September 2002) is acknowledged.

Claims 1-4 and 22-23 are under consideration in the instant application.

Specification

1. The disclosure is objected to because of the following informalities:

1a. An updated status of the parent nonprovisional application should be included in the first sentence of the specification. A statement reading "This is a continuation-in-part of U.S. Application No. 09/471,549, filed December 23, 1999, now abandoned..." should be entered.

1b. Patent applications are referenced throughout the disclosure (pg 9, lines 7, 19; pg 20, line 32). The status of the applications must be updated.

1c. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (see page 62, line 30). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

1d. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: "METHOD OF MODULATING MOVEMENT OF A CELL WITHIN THE SKIN OF A MAMMAL BY ADMINISTERING A CTACK ANTAGONIST".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of impairing movement of a CLA+ memory T cell within or to the skin of a mammal, said method comprising locally, topically, intradermally, or transdermally administering to said mammal an effective amount of an antibody against CTACK, wherein said antibody impairs movement of a cutaneous lymphocyte-associated antigen (CLA)+ memory T cell within or to the skin of a mammal, does not reasonably provide enablement for a method of modulating movement of a cell within or to the skin of a mammal, said method comprising administering to said mammal an effective amount of an antagonist of cutaneous-T-cell-attracting chemokine (CTACK). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1-4 are directed to a method of modulating movement of a cell within or to the skin of a mammal, said method comprising administering to said mammal an effective amount of an antagonist of CTACK. The claims also recite that the modulating is blocking and the

administering is an antagonist of CTACK. The claims recite that the movement is within the skin, the administering is local, systemic, topical, subcutaneous, intradermal, or transdermal. The claims recite that the cell is a CLA+ cell or said cell moves into the dermis and/or epidermis layers of the skin. The claims recite that the antagonist is an antibody which neutralizes CTACK, the mammal is subject to a transplant or skin graft, and the antagonist is administered in combination with an antibiotic.

The specification teaches that BALB/c mice are treated with 0.5% di-nitrofluorobenzene (DNFB) on the shaved abdomen. One day five and six, the mice receive intraperitoneal injections of neutralizing antibodies against mCTACK. Two hours after the injection, mice are challenged with 0.2% DNFB on the left ear and ear swelling is monitored (pg 78, lines 23-30). Histological analyses indicate a reduced skin thickness in anti-mCTACK-treated mice and monitoring of challenge-induced ear swelling confirms a significant suppression of skin inflammation in anti-mCTACK-treated mice when compared to mice injected with isotype control (pg 80, lines 13-18). Furthermore, the specification teaches that draining lymph node and spleen cells of sensitized BALB/c mice are labeled with CFSE and transferred into naive mice, pretreated with neutralizing anti-mCTACK or isotype before contact allergen challenge (pg 80, lines 26-30). Extraction and quantification of skin-infiltrating CFSE+ lymphocytes from allergen challenged mouse ears show anti-mCTACK treated mice have about 37% less CFSE+ skin-infiltrating lymphocytes compared to isotype control (pg 81, lines 2-3). The specification also discloses that analyses using a total lymphocyte gate indicate that anti-mCTACK treated mice who receive adoptively transferred cells show about 31% lymphocytes present in the skin compared to isotype-treated control mice (pg 81, lines 4-6).

However, the specification of the instant application does not teach administering to a mammal all possible antagonists of CTACK, other than an anti-CTACK antibody. Furthermore, since the specification provides no guidance regarding what sort of compounds should be screened for the desired antagonistic activity, the skilled artisan must resort to trial and error experimentation to determine which class of compounds might yield one with the desired activity. Such trial and error experimentation is considered undue. A large quantity of experimentation is also required by one of skill in the art to administer all possible CTACK antagonists to a mammal or patient and determine the optimal dosage, duration, and mode of administration of those antagonists. The specification also does not teach the modulation or blocking of movement of all cells within or to the skin of a mammal. Undue experimentation would be required of the skilled artisan to modulate or completely block movement of all possible cells within or to the skin a mammal upon administration of a CTACK antagonist. It is noted to Applicant that the term "blocking" in claim 2 is interpreted as meaning that an activity will not occur, i.e. movement of a cell within or to the skin will not occur. The specification also does not teach any methods or working examples that indicate any CTACK antagonist modulates the movement of a cell in the skin of a mammal that is subject to a transplant or skin graft or that the CTACK can be administered in combination with an antibiotic. The present invention is unpredictable and complex wherein one skilled in the art may not necessarily modulate or block movement a cell within or to the skin of a mammal by administering an antagonist of CTACK.

Furthermore, the specification does not disclose that a CTACK antagonist is administered systemically to a mammal. Overall, relevant literature reports that the goal of delivering proteins and peptides noninvasively has only achieved modest success, with poor applicability to proteins

and peptides (pg 343, col 1-2; Pettit et al. Trends Biotechnol 16: 343-349, 1998). The problems posed by proteins and peptides is their large molecular size, electrical charge, relatively hydrophilic nature, and relative instability in environments of extreme pH or proteolytic activity (such as the stomach and intestine) (pg 343, col 2). Pettit et al. review several routes of protein administration and the limitations that have been encountered. For example, proteins or peptides administered systemically must resist clearance via molecular filtration by the kidney and clearance by the reticuloendothelial system (pg 345, col 2). Therefore, the state of the prior art establishes the unpredictability of systemically delivering proteins to a mammal.

Due to the large quantity of experimentation necessary to identify all possible CTACK antagonists and to administer those antagonists to a mammal and to modulate the movement of all possible cells within or to the skin, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to the same, the complex nature of the invention, and the state of the art which establishes the unpredictability of delivering proteins to a subject, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

3. Claims 22-23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 22-23 are directed to a method of treating a patient suffering from a skin disorder comprising administering an effective amount of an antagonist against CTACK, wherein the antagonist is an antibody.

As discussed above, the specification teaches that BALB/c mice are treated with 0.5% di-nitrofluorobenzene (DNFB) on the shaved abdomen and then receive intraperitoneal injections of neutralizing antibodies against mCTACK. The specification also teaches that draining lymph node and spleen cells of sensitized BALB/c mice are labeled with CFSE and transferred into naive mice, pretreated with neutralizing anti-mCTACK or isotype before contact allergen challenge (pg 80, lines 26-30). However, the specification does not disclose treating a patient suffering from a skin disorder by administering an antagonist against CTACK. Although the specification teaches that CTACK mediates recruitment of T cells to cutaneous inflammatory sites and antagonists may be useful in the treatment of medical conditions or diseases associated with immunological conditions of the skin, this is not adequate guidance, but is merely an invitation for the artisan to use the current invention as a starting point for further experimentation (pg 24, lines 22-27). One skilled in the art cannot predict from the examples in the specification that the movement or impairment of movement of cells in the skin is indicative of a treatment for a skin disorder. The specification also provides no guidance regarding what skin disorders should be treated by a CTACK antagonist and the skilled artisan must resort to trial and error experimentation to determine which skin disorders can be treated by all possible CTACK antagonists. Such trial and error experimentation is considered undue. As discussed above, the specification of the instant application also does not teach administering to a patient all possible antagonists of CTACK, other than an anti-CTACK antibody. The present invention

is unpredictable and complex wherein one skilled in the art may not necessarily treat a patient suffering from a skin disorder by administering an antagonist of CTACK.

Due to the large quantity of experimentation necessary to identify all possible CTACK antagonists and to administer those antagonists to a patient to treat all possible skin disorders, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to the same, the complex nature of the invention, and the unpredictability of treatment of a skin disorder, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-4 and 22-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. Regarding claims 1-4 and 22-23, the acronyms "CTACK" and "CLA+" render the claims vague and indefinite. Abbreviations should be spelled out in all independent claims for clarity.

6. Claim 3 is indefinite because the elements recited in the claim do not constitute proper Markush groups. The claim is indefinite in the alternative use of "and/or" because it is not clear what controls which of these limitations. See MPEP § 2173.05(h).

7. Claims 1-4 are indefinite because the claims do not have a step that clearly relates back to the preamble. For example, there is no step indicating that movement of a cell within or to the skin of a mammal occurs after administration of the CTACK antagonist.

Conclusion

No claims are allowable.

The art made of record and not relied upon is considered pertinent to applicant's disclosure:

Homey et al. Nat Medicine 8(2) : 157-165, 2002.

Kunkel et al. Immunity 16 : 1-4, 2002.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (703) 305-7148. The examiner can normally be reached on 8:30-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 872-9305.

BEB
Art Unit 1647
November 26, 2002

Bridget C. Bunner